CONCERNING VASOMOTOR AND TROPHIC DISTURBANCES OF THE UPPER EXTREMITIES; WITH PARTICULAR REFERENCE TO THROMBO-ANGIITIS OBLITERANS.

By Leo Buerger, M.D.,

ASSOCIATE ATTENDING SURGEON AND ASSOCIATE IN SURGICAL PATHOLOGY, MOUNT SINAI HOSPITAL; VISITING SURGEON, HAR MORIAH HOSPITAL; INSTRUCTOR IN CLINICAL SURGERY, COLUMBIA UNIVERSITY,
NEW YORK.

It is not generally known to clinicians that certain well-recognized vasomotor and trophic disturbances of the extremities may, on the one hand, be the clinical manifestations of occluded vessels, and may also, on the other hand, be associated with arteries and veins that are organically intact. To the latter group belong those interesting symptom complexes which have been described under the name Raynaud's disease, erythromelalgia and acroparesthesia, multiple neurotic gangrene, scleroderma, sclerodactyly, and chronic acro-asphyxia. Considerable attention has been focussed upon these conditions, and attempts have been made to differentiate various discrete syndromes under the above-mentioned appellations. It is conceded that all have one feature in common, *that the arteries and veins have suffered no organic alteration in their patency.* Comparatively little, however, has been written to show that there is a distinct clinical and pathological entity, *thrombo-angiitis obliterans*, with which there may be associated clinical manifestations almost identical with those that belong to these other diseases. It is of no little importance to be aware of this fact and to be able to recognize that there is a disease whose symptoms depend upon vascular occlusion, for the prognosis and treatment of the two types of affections are in no way identical.

A clinical study of 200 cases of thrombo-angiitis obliterans during the last eight years (1906 to 1914) has enabled me to watch the course of this remarkable disease through all its clinical stages. Many of the cases have been followed from five to eight years, and the presence of interesting mutations in the symptomatology could be recorded. It was found that in a certain number of the patients *the upper extremities are involved, although it is usually believed that only the lower extremities are affected. And particularly* here were patients' histories encountered that singularly emphasized the unreliability of clinical signs alone in diagnosis. Furthermore, as shall be shown in some instances, thrombo-angiitis may, by virtue of the predominance of certain objective phenomena, masquerade as almost any of the true vasomotor and trophic diseases. Yet a careful study of each and every case will almost always make possible the recognition of the nature of the morbid process.

It may be of some clinical interest, therefore, to present here (1) the most striking examples of the various forms in which the disease may affect the upper extremities, where thrombo-angiitis obliterans is most frequently mistaken for other affections, and (2) to point out upon what features the diagnosis of the malady may be made.

A survery of the histories shows that the upper extremities may be clinically involved in the following ways: (1) without subjective symptoms; (2) with vasomotor symptoms predominating; (3) with trophic disturbances alone; (4) with gangrene of slight extent; (5) with extensive gangrene threatening the viability of the extremity; (6) with extensive atrophy of the hand and forearm; and (7) with changes simulating scleroderma and sclerodactyly.

I. THROMBO-ANGIITIS OBLITERANS OF THE UPPER EXTREMITIES WITHOUT SYMPTOMS. Just as in thrombo-angiitis of the lower extremities, there are cases in which the radial or ulnar artery, or both, become gradually closed without the patient's experiencing any noticeable symptoms. In some instances, absence of pulsation was discovered during a routine physical examination; in others, where symptoms were present in the lower extremities, investigation of the radial and ulnar vessels had demonstrated their occlusion.

CASE I.—J. A., male, aged forty years, Russian, began to have trouble in the right leg ten years ago (1904), pain coming on during walking, subsiding when at rest. Gangrene of the little and of the big toes developed, leading to amputation of the leg at its middle in 1906. Since 1908, similar symptoms involved the left leg, and the first and second toes became ulcerated, also requiring amputation. During the period of clinical observation the right radial pulse gradually disappeared, although no vasomotor or trophic manifestations could be elicited on examination. The patient was lost sight of so that the further course could not be followed.

The symptoms of Raynaud's disease, too, may be closely mimicked, as in the following cases:

II. CASES IN WHICH VASOMOTOR PHENOMENA PREPONDERATE. Such an instance is described in the following history, where, after about ten years of migrating phlebitis, and the usual circulatory disturbances of the lower extremities, distinct evidences of involvement of the vessels of the arm and hand supervened.

CASE II.—A. B., male, aged thirty-one years, Russian, noticed the appearance of small hard lumps under and in the skin of the calf of both legs in 1904 (ten years ago). They were painful, lasted for a few days or a week or more, and would then disappear (migrating phlebitis). For three years similar lumps and strands would come and go over the lower and inner side of the right thigh. About seven years ago he began to experience cramp-like pain in the right foot and calf of the leg on walking. Later the right foot became "cold." An ulcer developed on the third toe and showed no tendency to heal.

For seven years he has been suffering with similar symptoms in both legs and feet, the typical symptoms of pulseless vessels, erythromelia, ischemia in the elevated position, and gangrene of several toes being present. He now (1914) has already lost four toes of the left foot and two of the right.

Four months ago his right hand began to trouble him. In cold weather it would become very pale, particularly the little finger. On warming the hand, color would gradually return. Of late, however, the tip of the little finger has been bluish for days at a time, although excessive heat seems to bring back a normal color.

Physical Examination, May 6, 1914. The radial and ulnar arteries of both sides pulsate distinctly. Both hands perspire profusely, and are somewhat cold. The tip of the little finger of the right hand is cyanotic and deeply discolored over its palmar aspect. Pressure over this part elicits some pain. Roentgen-ray examination of the hand is negative.

On July 31, 1914, patient says that the little finger and thumb of the right hand feel cold. Scales form on the tip of the little finger, and when these separate, leave a healed depression. He has no pain.

Physical examination shows that both the little finger and the thumb are distinctly cold to the touch, the coldness extending to the base of the fingers. The other hand and fingers are warm. The radial and ulnar arteries pulsate well. On elevation there is no appreciable change in the color of the fingers.

In short we have here an example of thrombo-angiitis in which vasomotor symptoms initiate the onset of the disease in the upper extremities. Previous experience warrants the assumption that we may either expect a complete cessation of the symptoms in the hands, if adequate collaterals be established, or progressive occlusion of vessels until the radial and ulnar arteries become obliterated or until gangrene ensues.

CASE III.—J. V., male, aged thirty-four years, Russian, admitted to the Mt. Sinai Hospital (Dr. Lustgarten's service) December 17, 1907, says that three and a half years previously he noticed that his fingers were cold but not blue. The following winter the same symptoms returned, but, in addition, the skin of the tip of the right middle finger became dry and a "wound" spontaneously developed. For the past two years his hands would get blue, cold, and numb on exposure to cold, their natural color returning in a warm room. There was never any pallor. A sort of "sticking" pain in the finger tips would regularly accompany the state of blueness.

Physical Examination, December 17, 1907. Both hands are deeply cyanotic up to the wrist, and very cold. During the examination bright-red or crimson-colored spots can be seen to appear in the dorsum and palm. Over the back of the hand these red blotches become very distinct and do not shade off into the blue areas. The two distal phalanges remain deep blue. If the hands be observed for a still longer time (five minutes) the red color becomes paler and is mottled with a yellowish-pink; at times a totally different and much lighter shade, variegated with red and blue, will completely replace the deep colors first noted. In the palm the red areas are not so apparent, but they also give way at times to the lighter shades. The terminal phalanges of the ring fingers are enlarged, those of the middle fingers somewhat less so. When the hands are held above the head for two or more minutes the redness disappears, a pale sickly purple remaining. The radials and brachials pulsate well.

In the lower extremity a similar picture is present, but there are evidences of obliteration of the vessels. The right dorsalis pedis cannot be felt, although palpated on many occasions from December 17, 1907, to January 20, 1908. In the left dorsalis pedis there is fair pulsation. There is ischemia in the elevated position of the legs, as evidence of the impaired vascular supply, and bespeaking the presence of the lesion, thrombo-angiitis.

If such an exquisite example of vasomotor disturbance can belong to a case of thrombo-angiitis obliterans, there is little wonder that confusion should exist in the differentiation of the symptoms due to neurogenous and organic lesions of the vessels. What the distinguishing points are upon which the diagnosis must be based will be discussed later in the paper.

III. CASES WITH TROPHIC DISORDERS ONLY. In some patients, distinctive signs of an affection of the upper extremities manifest themselves as trophic disturbances not extensive enough to lead to gangrene. The disease may be wholly overlooked by the patient and, when the lesion has healed, it may be subsequently referred to by him as a slight "sore" or "ulcer" developing without cause. Were it not for the presence of the disease in the lower extremities and for the changes in the radial pulse the nature of the trophic disorders would be difficult of solution.

CASE IV.—T. S., aged thirty-one years, Russian, consulted me in May, 1914, because of the condition of his left foot. Three and a half years previously he experienced pain in the sole of the left foot on walking and was treated for rheumatism. Two years after the onset a sore developed between the fourth and fifth toes of the left foot and another one on the tip of the big toe of the left foot. Since then the foot became red and the little toe gangrenous, falling off about a year ago. About this time his right leg began to trouble him, the symptoms being pain in the calf on walking.

Two and a half months ago there developed a spontaneous ulcer over the middle phalanx of the right hand, not accompanied by any evidence of inflammation, hardly painful, and not brought about by any injury. . He was treated for this for about eight weeks, when the wound healed.

Physical Examination, May, 1914. Over the middle phalanx of the right hand there is an irregularly shaped scar, about 8 mm. in length and 4 mm. in width, evidently the site of the old healed lesion. The right radial pulse is not perceptible.

We have here a typical case of thrombo-angiitis of the lower extremities, first involving the left then the right lower extremity, and three years later manifesting itself also in the hand, with trophic disturbances and obliteration of the radial artery.

IV. CASES WITH GANGRENE OF SLIGHT EXTENT. Not a small number of the patients that suffer with occlusion of the vessels of the upper extremities come to us with a history of having had pain in the tip of one of the fingers for a considerable time. This is followed by a change in the color of the skin, usually reddening of the tip of the fingers, as if it were inflamed. Later there develops a sore or the skin changes color and becomes gangrenous, usually at the tip of a finger, although the lateral margin of the finger may be first affected. The following three cases are examples of this group:

CASE V.—L. B., aged forty-eight years, Russian, male, admitted to Mt. Sinai Hospital (Dr. Lilienthal's service), May 1, 1910, says that his left leg was amputated below the knee some ten years ago. Six years later he lost his right leg in the same way. Now for six months the index finger of the left hand has been painful and red at the tip; this has since improved. Four months ago the index finger of the right hand also became red and painful, and during the last three weeks the greater part of the last phalanx has become mortified.

Physical examination shows an old scar at the tip of the left index finger and poor radial and brachial pulse. The terminal phalanx of the right index finger is completely exposed, the dry bone presenting. On elevation of the right hand, marked ischemia occurs.

The right radial pulse is absent, the brachial only faintly pulsating. The gangrenous process is evidently progressing, since a portion of the second phalanx is already involved.

CASE VI.—D. B., aged thirty-five years, male, Russian, first examined by me on July 16, 1904, at Mt. Sinai Hospital. He had been treated in the hospital eight years previously for "phlebitis" of the right leg. A portion (five inches) of a large vein was diseased at that time, the history recording that the process was "migrating," moving up and down the thigh. He says that this trouble lasted off and on for two years. In 1903 there were "lumps" in and under the skin of the righ leg and then three months later in the left leg. Such swellings would last a week, develop into hard, "tender spots," with a covering of red skin, and on one occasion three such spots appeared on the left arm in front of and just below the elbow.

Physical Examination, July, 1904. In the left antecubital region there is a thickened, slightly reddened cord about two inches long. Another is situated on the ulnar aspect of the same forearm near the elbow. The right forearm presents a similar vein about three inches from the elbow; the skin is not reddened. On the inner side of the right cubital space a subcutaneous, adherent nodule can be felt; it is very tender. There are several such nodules in the right calf and smaller ones over the left shin bone. No edema, but slight cyanosis of both legs in the pendent position. A portion of one of the thrombosed arm veins was extirpated for study.

Course. A year later (1905) symptoms referable to an affection of the deep vessels of the left lower extremity manifested themselves, namely, coldness and blueness of the left foot and superficial ulcers on the toes. In February, 1907, he developed a gangrenous patch at the tip of the middle finger of the right hand. His doctor had been treating him for a "felon" of the middle finger of the right hand. His hand had been cold for several weeks and the middle finger painful. Four weeks previously a black, "dead" spot appeared at the tip of the finger, and since then, what with cutting it and self-treatment, he thought that the present intensely painful affection had overtaken him.

Physical Examination, February 1, 1907. A portion of the tip of the middle finger is gangrenous; there is no infection; the distal phalanx seems to take part in the process of mortification.

On holding both hands above the head for some time the right becomes appreciably more ischemic than the left; it does not attain the cadaveric hue characteristic of the lower extremities, but becomes markedly pale, a bluish-red tinge remaining in the distal phalanges. The pain is not increased in this portion. In the dependent position the color rapidly deepens in the left hand, soon assuming a reddish-blue hue, the fingers being particularly discolored. Both radial pulses are felt, the left somewhat small. On the dorsum of the hand, just over one of these veins, there is a bean-sized, indurated area; the skin over it is adherent and tender. About one inch above the wrist, behind the radius, there is a reddened, hard cord more than an inch in length (doubtless a thrombosed vein). The finger improves very slowly.

Here there is most beautifully illustrated that group of cases in which a long period of "migrating phlebitis," first of the lower and then of the upper extremities, dominates the clinical picture. Then, when the signs of impaired circulation of the legs have become well established, the hands, too, show unequivocal marks of the closure of small distal arteries, in the form of small areas of gangrene.

Case VII.—M. S., aged forty-seven years, Russian, was admitted to Mt. Sinai Hospital on June 25, 1907, giving the following history: About eight or nine months ago he noticed that the fourth toe of the left foot was cold, blue, and painful. About four months ago the pain became so severe that he consulted a physician, who told him that an infection had taken place. Since this time a sore developed under the nail and the nail bed became black.

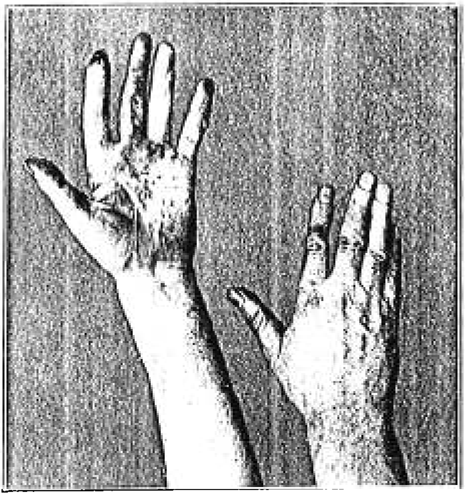


Fig. 1.—Trophic changes in index finger of Case VII.

Physical examination showed complete gangrene of the distal half of the fourth toe of the left foot, absence of pulsation in the dorsalis pedis artery, an area of superficial gangrene of the skin on dorsum of the foot, intense erythromelia (hyperemia of the foot) in the dependent position, and marked ischemia in the elevated position. June 28, 1907, amputation was done by Dr. J. Wiener through the tarsometatarsal articulation. On July 5, re-amputation was done through the middle third of the leg, the wound healing slowly.

In 1910 the disease began to involve the right leg in the same typical manner, leading also to dry gangrene of the fourth toe. When examined in March the popliteal, posterior, tibial, and dorsalis pedis of the right leg could not be felt.

In short we have a typical case of thrombo-angiitis obliterans, first involving the left lower extremity leading to gangrene, amputation, and some three years later involving the right leg.

In March, 1914, I again saw the patient, who now complains of symptoms in the left hand.

March 18, 1914. For several months he has had pain in the tip of the left index finger and lately the finger has changed color, becoming withered and glossy.

Physical examination shows an ulcer at the tip of the left index finger, the live skin above it atrophied and glossy, the hand somewhat smaller than the other, and the fourth finger of the same hand distinctly shrunken. The radial pulse of this hand cannot be felt (Fig. 1).

We are evidently dealing here with a case in which some seven years after the onset of the disease in the lower extremities the left upper extremity became attacked, as evidenced by ulceration and trophic disturbances.

An interesting group is formed by those patients in whom trophic disturbances and gangrene are the salient features. These are the cases so often confused with Raynaud's disease. In our experience the lower extremities are regularly involved at some time or other, and it is, therefore, necessary to watch carefully for the advent of the typical symptoms in these, so that a correct interpretation of the phenomena in the fingers and hands may be made. The following two histories will well illustrate the cases in which:

V. EXTENSIVE GANGRENE THREATENS THE VIABILITY OF THE EXTREMITY. CASE VIII.—A. K., male, aged twenty-seven years, Russian, was admitted to Mt. Sinai Hospital January 4, 1908. About two years previously he had had severe pain in the middle finger of the right hand. The finger became cold, at times very blue, and extremely painful. These symptoms persisted for about two months, when he was told to have the nail removed. Shortly after this was done the tip of the finger became dry and black. After several months the terminal phalanx separated spontaneously, but a wound remained which refused to heal.

For about two months his left hand has been affected, there being excruciating pain in the left middle finger of the left hand, and the fourth finger of the right hand also being somewhat painful for two months. He thinks that the tip of the middle finger of the left hand first became dark blue or purple, and lately has become dry and black.

Physical Examination, January 4, 1906, shows that the distal phalanx of the middle finger of the right hand is absent, the tip of the fourth finger showing a small patch of dry gangrene of the left hand; there is beginning gangrene of the distal phalanx of the middle finger.

Somewhat more than a year later, February 24, 1907, he was again admitted to the hospital, presenting evidences of thrombo-angiitis of the left foot. The second toe of the left foot had been ulcerated for about three months, and gradually all the toes of that foot, except the fourth, became involved in the same process.

Physical Examination, February 24, 1907. Left foot: On the dorsal and plantar surfaces of the great toe there are ulcers. A similar condition is found at the tip of the second toe and on the plantar and dorsal surfaces of the fifth toe. The skin about the ulcer is sloughing and shows no tendency to heal.

The right foot is negative. The right hand shows an absence of the terminal phalanx of the third finger. Both hands are cyanosed.

March 22. Amputation of the toe. Wound does not heal.

May 17. Re-amputation through the leg, by Dr. C. Elsberg.

Physical Examination, May 20, 1907. The left radial pulse is absent and the artery appears to be converted into a hard cord. In the right radial artery a very faint pulse is perceptible. The brachial artery seems to be much thickened, although the pulsation is good. Ever since amputation of the left leg was done, the stump was painful, discolored, bluish, presenting a wound that failed to heal. Finally, on January 2, 1909, the patient consented to re-amputation. I performed the Gritti-Stokes amputation, the stump healing kindly.

January 3, 1909. The tip of the little finger of the right hand presented a small spot of gangrene about 1 cm. in diameter. The distal phalanx of the little finger is absent. The nail of the fourth finger is deformed and thickened. In the dependent position the fingers become cyanotic, with a slight increase in the normal red color. The left hand is normal as regards color, but the nail of the middle finger as well as the tip of the finger are very much deformed.

The right radial artery is felt as a cord, and no pulse can be detected; the ulnar artery is also pulseless; the brachial pulse is poor. The left radial artery is faint, the ulnar cannot be felt, the brachial also is poor. In the elevated position the right hand becomes somewhat paler than the left, but neither becomes very much blanched.

Lower extremity: The stump is in good condition. The right foot shows evidences of development of thrombo-angiitis, the dorsalis pedis and posterior tibial arteries being absent, and there are other evidences of involvement of that leg.

December 30. The fifth finger of the right hand presents an ulcer at the tip, the result of the separation of a gangrenous patch. He says that he has had pain in that finger for about three months, and that gangrene set in about three weeks ago.

February, 1910. The trophic disturbances, involving the little finger of the right hand seem to be progressive. The tip of the finger shows advancing gangrene, the rest of the finger is swollen and red. In the dependent position the third and fourth fingers become intensely red and slightly cyanotic. Left hand: Here there has been no progression of the symptoms.

FIG. 2

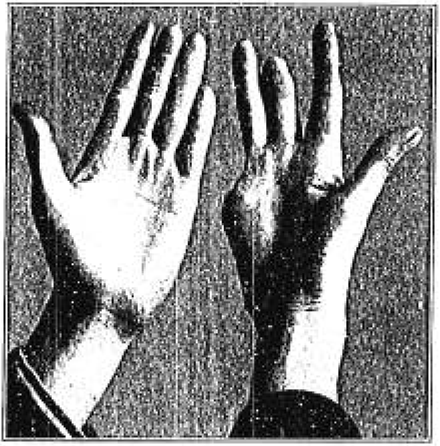
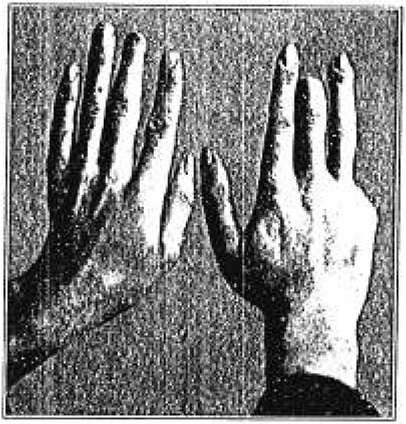


FIG. 3



FIGS. 2 and 3.—Hands in Case VIII, results of gangrene and amputation.

February 2, 1910. The little finger of the right hand was amputated (Figs. 2 and 3).

This is a good illustration of those cases of thrombo-angiitis obliterans in which the symptoms first make their appearance in the upper extremities, are initiated by pain, and followed by trophic disturbances and gangrene. In this case the terminal phalanx of the middle finger and the whole of the little finger of the right hand were lost. During the evolution of these symptoms the disease attacked the left leg, where even greater progress was made than in the upper extremities, amputation being the outcome. Pathological examination of the vessels of the amputated left limb showed the usual lesions of thrombo-angiitis obliterans.

Case IX.—S. A., male, Russian, examined March 23, 1905, gives a typical history of thrombo-angiitis obliterans of the left lower extremity, finally leading to gangrene, for which the leg was amputated August, 1903, and re-amputated September 5, 1903, at the knee.

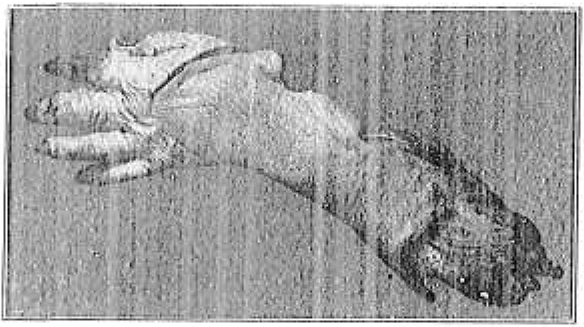


Fig. 4.—Amputated arm of Case IX. (Photograph taken from specimen after preservation in fixative.)

Eight weeks before admission there appeared symptoms referable to the same disease of the right lower extremity, an ulcer appearing at the inner side of the right heel. On March 21, 1905, the right leg was amputated for advancing gangrene of the right foot.

March 10, 1910. I found evidence of the involvement of the left upper extremity. He says that he has had trouble in his left arm and in the fingers and forearm for several months, there having been pain in the fingers, followed by swelling and redness. Then a bleb appeared at the tip of the index finger, which was incised by a physician. Shortly after this the wound became much worse and sloughing took place. About the same time a black spot appeared over the back of the middle finger. Neither middle nor index finger has improved, and it is for these that he seeks relief.

After admission the gangrene rapidly spread, the pain becoming excruciating, and the forearm was amputated through its upper fourth.

The ablated forearm (Fig. 4) showed complete occlusion of both radial and ulnar arteries. The typical lesions of thrombo-angiitis obliterans were present.

Four years later, April, 1914, the patient was again admitted to the wards of Mt. Sinai Hospital in a condition of stupor. The notes taken read as follows: "Both legs and the left arm have been amputated. Speech is incoherent and there are evidences either of some cerebral lesion or of an arterial lesion in the brain. The condition of the right hand is of particular interest. Nowhere is there any evidence of ulcer or gangrene. The skin of the right hand is dry and atrophic. The fingers have a tapering apperance. The skin has lost its elasticity, the subcutaneous tissues have withered, and neither the radial nor the ulnar arteries are palpable. The brachial artery, too, gives but the slightest impression of the presence of pulsation."

Here, then, is a case in which two distinct clinical pictures were evolved in the course of the obliterative vascular disease, one exhibiting gangrene of an upper and two lower extremities, and the other demonstrating the unusual phenomenon of extreme atrophy of both hands and forearm.

VI. CASES SIMULATING SCLERODERMA AND SCLERODACTYLY. Perhaps most interesting of all are those cases in which the vascular occlusion has led, by virtue of the effects of malnutrition, to a condition of dystrophy, the clinical picture being akin to that of sclerodactyly. In fact we have had occasion to observe a most pronounced example of this manifestation in a patient in whom the diagnosis of scleroderma was made by expert dermatologists.

CASE X.—I. L., aged thirty-five years, was admitted to the surgical service of Mt. Sinai Hospital on October 1, 1906, with a typical history of thrombo-angiitis obliterans of the left leg. There was absence of pulsation in the dorsalis pedis and complete gangrene of the second toe, necessitating amputation. Pathological examination of the vessels of the amputated legs showed the typical lesions of thrombo-angiitis obliterans.

June 29, 1907. He was again admitted to the hospital, complaining of intense pain in the right leg which showed the symptoms of ischemia on elevation, redness in the dependent position, but no evidence of trophic disorder or gangrene. The patient begged that the limb be taken off, and the right leg was, therefore, ablated through the middle third. Pathological examination showed here, too, the typical lesions of thrombo-angiitis obliterans.

December 17, 1909. He entered the hospital complaining of trouble with his right hand and arm. For several months he has been unable to use it properly, the muscles having become stiffened. He thinks, too, that a marked diminution of the size of the hand and arm has taken place.

On physical examination the picture presented by the right arm is striking. The fingers have the typical appearance of the skin in scleroderma. Motion of the distal phalangeal joints is markedly impaired in extent. The skin is atrophic and dry and the circumference of the fingers of the right hand is distinctly diminished. Both the radial and brachial pulses are absent. The brachial artery can be felt as a hard cord, and can be traced as far as the axilla. In the axilla there is a distinct pulse.

The left hand shows no trophic disturbances, no ulcers, but the radial and ulnar pulses are absent. The brachial pulse is fairly good.

In order that we may thoroughly comprehend the points that distinguish the vasomotor and trophic disturbances dependent on organic arterial lesions from those of Raynaud's and allied diseases it may be best to pass rapidly in review the salient features of the symptomatology as they were exemplified by the above patients.

Collecting the cases in which vasomotor symptoms predominate we have, on the one hand, those in which the symptoms of thrombo-angiitis obliterans of the lower extremities are well marked and, on the other hand, those in which we are compelled to investigate very carefully in order to elicit evidences of vascular occlusion.

The symptoms simulating Raynaud's disease and acro-asphyxia are cyanosis of the finger tips, coldness of the fingers with or without trophic disturbances, and alternating cyanosis and rubor, involving the fingers or the whole hand. Rather characteristic in the symptomatology of thrombo-angiitis is the apparent dependency of the vasomotor symptoms upon variations in temperature, the chronicity of the manifestations, the absence of pain in some of the cases, and the absence of paroxysmal nature of the attacks so characteristic in Raynaud's disease.

When we turn to those patients in whom the trophic disturbances seem to be unassociated with evidence of vasoconstriction and vasodilatation we note that there is merely a history of the development of a spontaneous ulcer of the fingers. It seems more than likely that in many of these the history of the absence of the vasomotor phenomena would be found unreliable if it were possible to observe the cases throughout the whole course of the disease. Future observations will probably support my belief that here, too, some manifestations of deranged vasomotility do occur.

When we consider the largest group, namely, that in which gangrene of small or greater extent develops, we find that some cases may be mistaken for simple paronychia. Others claim that the development of a gangrenous patch or of the felon was preceded for a long time by distressing pains in the tips of one or more fingers. The vasomotor symptoms may be absent or the cyanosis and redness may be quite striking. The following sequence of symptoms may be observed and is interesting, because pain and trophic disturbances alone are complained of. The onset is marked by severe pain in the tip of a finger. This is superceded by atrophic changes in the skin, the development of a dry, hard patch, mortification, and also formation of an ulcer. In still other cases the similarity with Raynaud's disease is even more marked, for the symptoms are pain, cyanosis, rapidly followed by gangrene.

More rarely do we meet with those interesting examples of the effects of arterial occlusion in which the development of intense atrophy of a hand or limb or the production of the typical picture of scleroderma and sclerodactyly is the significant feature of the clinical picture.

A careful clinical study of the disease, thrombo-angiitis obliterans, will dissipate all doubt as to the possibility of separating this disease, as a clinical entity, from all those neurogenic varieties of vasomotor and trophic disorders that may be clinically confounded with it. It would be too extensive to dilate upon the symptomatology of thrombo-angiitis obliterans in this paper, and, therefore, I shall confine myself to the consideration of those essential features on which the recognition of the disease depends, and which will be seen to be the effects of the obliterated condition of the arteries.

Thus characteristic for the disease are the following groups of symptoms: (1) the disappearance of the pulses, particularly the dorsalis pedis, posterior tibial and popliteal, more rarely the femoral, radial, and ulnar; (2) the development of typical manifestations of impaired circulation, to wit: blanching of the lower extremities when these are elevated above the horizontal, hyperemia (rubor) or reddening of the foot in the pendent position (a chronic condition which I have elsewhere termed erythromelia) during certain stages of the disease, and trophic disturbances, such as impaired growth of the toe nails, slightly atrophic condition of the skin, ulcers, and gangrene; (3) true vasomotor phenomena of transitory nature, such as alternating syncope, rubor, coldness, apparently independent of those chronic changes that have been cited above and that are distinctly traceable to the occluded condition of the arteries and veins; (4) the symptoms of pain, either in the form of intermittent claudication (pain in the calf of the leg or in the foot on walking with cessation when the limb is at rest) or the severe pain that is associated with the advent of trophic disturbances, especially with ulcers and patches of gangrene; (5) the slow course of the disease, symptoms of intermittent claudication or pain, preceding the development of trophic disturbances for months and years; (6) the fact that more than 99 per cent. of the cases occur in Polish, Galician, or Russian Hebrews, and that almost always young males between the ages of twenty and thirty are taken with this disease; (7) the onset of symptoms in the lower extremities, one of the legs being first affected; (8) the comparative infrequency of involvement of the upper extremities; (9) the association of a peculiar type of migrating phlebitis in the territory of the external or internal saphenous, less frequently in the larger veins of the upper extremities characteristic in about 20 per cent. of the cases; (10) the slow but steadily progressive course, leading in a large majority of the cases to amputation of at least one limb, not infrequently of both lower extremities, and in rarer instances to amputation of one of the upper extremities as well.

Even a rapid review of the salient symptoms of this interesting malady would seem to suffice to leave the impression that it could hardly be mistaken for other diseases. And were it not for the fact that certain symptoms, closely resembling typical vasomotor phenomena, may persist for weeks and years in this disease, confusion with the true neurogenic vasomotor process would scarcely ever arise. The chronic condition of redness in thrombo-angiitis obliterans can be explained as due to dilatation of the superficial capillaries, this being a compensatory phenomenon making for an adjustment of the impaired circulation. This chronic redness or rubor may be mistaken for erythromelalgia or for the rubor of Raynaud's disease. The fact that it is associated with other evidences of closed vessels and the other characteristic features above mentioned, together with the circumstance that the redness disappears at once upon elevating the extremity, will make the recognition of its nature possible.

In addition to this more or less chronic or permanent sign of deranged vasoconstriction, other phenomena which are truly vasomotor in nature may frequently be associated in thrombo-angiitis, and it is these that must be differentiated from similar phenomena accompanying Raynaud's disease, erythromelalgia, scleroderma, sclerodactyly, and acrocyanosis.

If we do not overestimate the importance of single manifestations of vasomotor irritation, but regard as more significant the clinical course and the symptoms in their totality, we will not fail to separate very clearly in our minds the true vasomotor neuroses from the organic vascular disease attended with vasomotor phenomena.

In order that a differential diagnosis may be clearly presented, let us briefly recapitulate the typical course of a case of Raynaud's disease. Raynaud's disease is an affection whose pathology has not as yet been definitely determined, the lesion doubtlessly residing somewhere in the central nervous system. Its clinical characteristics may thus be summed up:[1] Somewhere in the peripheral portions of the body (so-called acra) there occurs more or less severe pain not confined to distinct nerve territory, usually affecting symmetrical parts, attacks of vasomotor disturbance being part of the syndrome. These latter are (1) syncope, asphyxia, or local rubor, and (2) severe trophic disturbances, usually in the form of gangrene of the parts first affected with symptoms. The course is an intermittent one, for there may be completely free intervals; but in some instances, evidences of disturbed vasomotility may persist. The disease may consume itself in one attack or several attacks may occur in succession. Objectively, sensory disturbances are usually absent, as well as paralysis, although other evidences of disturbed vasomotor innervation, such as aphasia, hemoglobinuria, arthropathy, may occur. Usually neuropathic individuals are affected. The organic vascular changes, as well as the lesions of the nervous system, reported occurring in some of the cases, have, doubtless, no causative relation with the disease.

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[1] Cassirer, Die Vasomotorisch-tropischen Neurosen (S. Karger, Berlin, 1912).

It is true that there are still some who cling tenaciously to the theory that some lesions of the peripheral arteries may account for the symptoms of Raynaud's disease. In support of this view certain anatomical findings have been cited as strong arguments by those who believe that a definite anatomical lesion in the peripheral vessels is irresistible testimony against pure hypothesis. A careful analysis of the cases in question, as made by Cassirer, shows that reported organic alterations in the vessels will not suffice to explain the symptoms any more satisfactorily than the theory of a central nerve affection of the sympathetic system. Whereas in thrombo-angiitis obliterans the territory manifesting symptoms corresponds to that containing the diseased vessels, we find that no such relation exists where vascular lesions are associated with Raynaud's disease.

For the clinical diagnosis of thrombo-angiitis we must depend upon (1) the racial (Hebrew) and sex (male) predilection; (2) the early involvement of the lower extremities; (3) the early symptoms of pain or intermittent claudication; (4) the presence of migrating phlebitis; (5) the evidences of pulseless vessels; (6) the presence of blanching of the extremity in the elevated position; (7) the existence of rubor in the dependent position; (8) the relation of the hyperemic phenomena to posture; (9) the absence of simultaneous, symmetrical involvement; and (10) the slow, progressive chronic course terminating in gangrene.

In Raynaud's disease we will note the following features: A sudden onset of the first stage of local syncope or regionary ischemia involving usually the fingers, more rarely the toes, and occasionally the margins of the ears or the tip of the nose with coldness and blanching; associated sensory phenomena, paresthesia, and pain; a comparatively short duration of the vasomotor and sensory manifestations, their intermittent character with return to normal between the attacks; the symptoms of local asphyxia attended with local depression of temperature and swelling of the parts involved; the disappearance of the asphyxia with substitution of reactive hyperemia and a third stage of dry gangrene. Characteristic for this disease as well as for the cases of scleroderma and sclerodactyly is the striking atrophy of the ends of the distal phalanges.[2] The changes in the bones can be well demonstrated by Roentgen-ray examination, atrophy and disappearance of large portions of the end-phalanges being distinctive and diagnostic features. In our own experience the alterations in the bones could be detected early in the disease, probably developing simultaneously with the other trophic disturbances.

If we analyze the symptomatology of the cases of thrombo-angiitis cited above we will find, that the differential diagnosis of this condition from the vasomotor neuroses is only difficult in those cases where we cannot rule out the possibility of the association of the two diseases. It will be noted that where coldness and cyanosis are complained of, a distinct dependency on temperature or other environmental condition can often be elicited or that pain is absent. The presence of vessels changes and the history of the involvement of a lower extremity at once clear up the diagnosis.

Where trophic changes alone are present, the absence of symptoms referable to the central nervous system speaks decidedly against nerve lesions. The relation of the vasomotor symptoms to the position of the limb will in other cases be of value in explaining the nature of the symptoms.

How can we explain the occurrence of true vasomotor phenomena such as do not seem to owe their existence to the mechanical effects of impaired circulation? The blanched appearance that is a sequence of an obstructive condition of the arteries, and which can be demonstrated by elevation of the leg, and in bad cases can even be elicited in the horizontal position, is a phenomenon easily explicable on the theory that the avenues of arterial supply are cut off through extensive obturation of the arteries. Many clinical and experimental observations have been gathered that speak in favor of this view. So also is the rubor not a true vasomotor phenomenon, but a sign of chronic vasodilatation of the superficial capillaries and is compensatory in nature.

On the other hand, veritable symptoms of disturbed vasomotility can be associated with thrombo-angiitis obliterans. That these should occur is not surprising when we call to mind that not only have intense and extensive destructive, pathological alterations taken place in the most important arteries of a limb, but that the accompanying nerves are frequently bound down by a dense mass of cicatricial tissue and have undergone severe fibrotic changes. Although the mechanism of the irritative and exhaustive vasomotor phenomena is not clear, the total disorganization of the vascular innervation in many of the cases would seem to afford sufficient basis for the possibility of the occurrence of the disturbances which we call "vasomotor" in nature.

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[2] Compare with changes in sclerodactyly (Figs. 5 and 6).

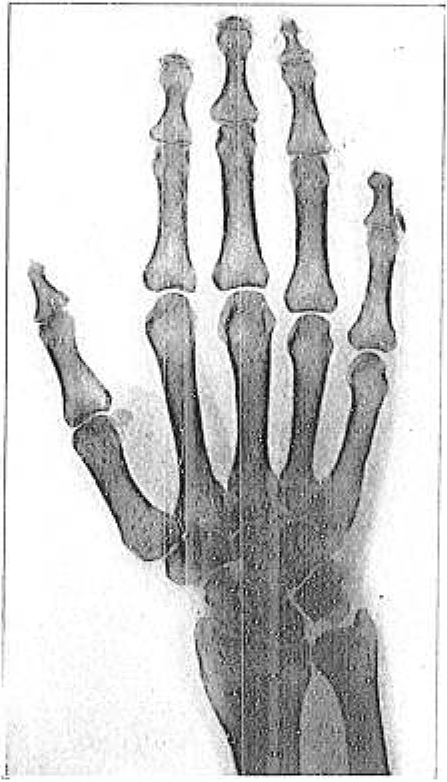

FIG. 5.—Roentgen-ray photograph of a case of sclerodactyly, showing disappearance of the terminal phalanges.

Where signs of thrombo-angiitis of the lower extremities are unquestionably present, and where evidences of vascular occlusion in the upper extremities are lacking, although these are the site of disturbed vasomotor innervation, we may for a long time be unable to rule out the possibility of the simultaneous occurrence of two different diseases.

The differentiation of true scleroderma from thrombo-angiitis will be rarely difficult to make. In scleroderma and sclerodactyly the first stage with hard edema is characteristic and never simulated by cases of organic vascular disease. The second indurative stage may, however, be almost exactly reproduced by other affections. The form of scleroderma known as "sclerodactyly," because of attendant alterations in the deeper tissues, may be not unlike

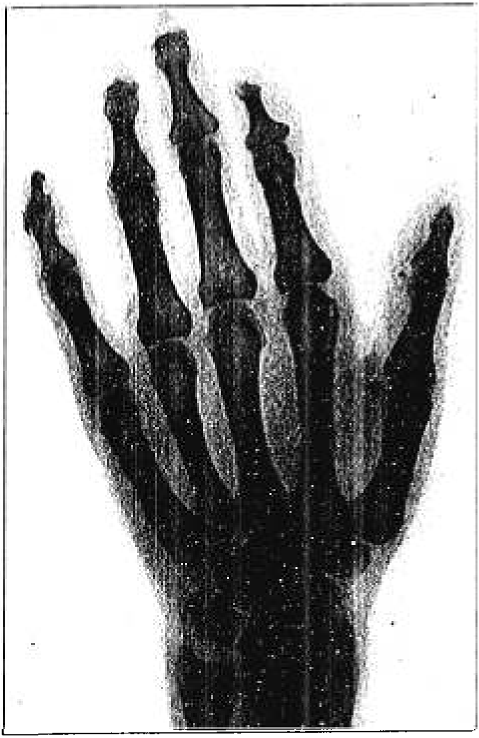

Fig. 6.--Roentgen-ray photograph of a case of sclerodactyly, showing disappearance of the terminal phalanges.

thrombo-angiitis. Roentgen-ray examination of the hand in sclerodactyly offers the most valuable means of differentiating the two diseases (Fig. 5 and 6). The phalanges will very early show atrophic changes and disappearance of the terminal portions in scleroderma, sclerodactyly, and Raynaud's disease, while the bones, although somewhat rarefied, will be seen to conserve their outlines throughout the course of the disease, thrombo-angiitis obliterans, until they are disturbed by the effects of gangrene.

So far as our experience permits us to judge, symptoms of scleroderma occur only late in thrombo-angiitis when other signs of vascular occlusion have already become well developed. The recognition of the condition will then depend upon the absence of pulsation in the larger peripheral vessels, the presence of gangrene (or the history of such a condition) and of the other typical signs of obliterated arteries and veins.

In the light of our recent studies on the pathology of thrombo-angiitis obliterans we are able to state that certain characteristic morphological changes in the arteries and veins are specific[3] for this process. These occur in the deep arteries and veins as well as in the superficial veins, when these are the seat of the so-called "migrating phlebitis." Whenever migrating phlebitis is present, therefore, the excision of a portion of vein under local anesthesia followed by microscopic examination will lead to a diagnosis.

It is most probable that in Raynaud's disease and the related affections the seat of the pathological process is to be sought in the vegetative system, that is, somewhere in the vasomotor apparatus. Nor are we likely to be rewarded in a search for any organic change. The frequent return to a normal condition, observed clinically, also speaks against the likelihood of morphological or chemical alterations in the nervous system.

Whereas in thrombo-angiitis obliterans a definite and specific morphological change in the arteries and veins is responsible for the varied phenomena in the superficial capillaries, in Raynaud's and allied diseases the vasomotor and trophic disturbances are the outcome of irritative and exhaustive processes of the sympathetic nervous system.

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[3] Surg., Gyn., and Obs., 1914.